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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/076,404	05/12/1998	DAVID J. ECKER	IBIS-0007	4802
27180	7590	06/25/2007		
ISIS PHARMACEUTICALS INC 1896 RUTHERFORD RD. CARLSBAD, CA 92008			EXAMINER BRUSCA, JOHN S	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 06/25/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	Application No. 09/076,404	Applicant(s) ECKER ET AL.	
	Examiner John S. Brusca	Art Unit 1631	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 11 June 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 11 June 2007. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see discussion below. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_  
Claim(s) objected to: \_\_\_\_\_  
Claim(s) rejected: 19, 20, 26, 30 and 32-47.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s): \_\_\_\_\_  
13. ☐ Other: \_\_\_\_\_.

*John S. Brusca 27 June 2007*

John S. Brusca  
Primary Examiner  
Art Unit: 1631

Continuation of 5. Applicant's reply has overcome the following rejection(s): the rejection under obviousness-type double patenting over Application Nol 10/104,949 in view of the abandonment of the application as noted in the applicant's response.

Continuation of 11. does NOT place the application in condition for allowance because: Regarding the lack of compliance with the sequence rules, the Office has not received a new paper copy of the sequence listing or a computer readable form. and the objection to the specification is maintained. The applicants state on page 10 of their remarks that claims 21-23, 26-28, and 31 are rejected for lack of written description, however the rejection only applies to claims 36-47. The applicants point to support for an interaction site that is less than 30 nucleotides in length at page 131, example 1 which shows a human IRE element. The IRE element is described as being approximately 30 nucleotides in length rather than less than 30 nucleotides in length. For this reason the rejection for lack of written description is maintained. It is agreed that the IRE element is shown to comprise an interaction site in an untranslated region, as claimed in claims 38, 41, 44, and 47, but those claims require the full scope of claims 37, 40, 43, and 46, which require an interaction site that is a bulge, a loop, a stem, or a mismatch repair which is not described in the context of the claims as a whole. Upon review of the specification, it is noted that page 133 discusses the IRE 5' UTR in figure 5, but it appears to be shown in figure 6 instead. The proposed amendment to claim 30 would overcome the rejection of the claim under 35 U.S.C. 112, second paragraph if entered. The arguments concerning the rejection under 35 U.S.C. 103(a) are based upon entry of the amendment and are therefore not persuasive in view of the non-entry of the amendment. .